*Intensive Care Med*
https://doi.org/10.1007/s00134-025-08124-4

**WHAT'S NEW IN INTENSIVE CARE**

# Delirium versus encephalopathy: a call for precise terminology

Katarzyna Kotfis[1*], John P. Kress[2] and Arjen J. C. Slooter[3,4*]

© 2025 The Author(s)

## Terminology: delirium versus encephalopathy

Research and clinical care are hampered by the use of numerous terms to describe global cognitive dysfunction due to critical illness [1]. These include delirium, (acute) encephalopathy, acute confusional state, acute brain dysfunction, acute brain failure, and altered mental status. Although there is no evidence that these different terms represent distinct clinical entities, literature on the most frequently used terms, delirium and encephalopathy is highly segregated (Fig. 1, left side) [2]. Delirium-titled articles rarely cite articles with encephalopathy as a title word and seldom mention encephalopathy in the text [2]. These articles are published preferentially in journals of geriatrics, gerontology, psychiatry, psychology, intensive care medicine, or anaesthesiology [2]. Similarly, encephalopathy-titled articles rarely cite papers with delirium as a title word, and rarely mention delirium in the text. These papers are published mainly in journals of neurology, neurosciences, general or internal medicine, or other fields, such as genetics [2].

To overcome problems due to segregation of the literature, a multidisciplinary international expert panel was formed to generate consensus recommendations using the modified Delphi method, which has been endorsed by ten major professional societies. The panel regarded acute encephalopathy to be the pathobiological process in the brain, and coma and delirium as possible phenotypic manifestations of this process (Fig. 1, right side) [2]. It did not recommend the ongoing use of the terms acute confusional state, acute brain dysfunction, acute brain failure, or altered mental status, as they lack precision and additive value [2].

Although these efforts were applauded, others criticized the lack of a term to identify a non-comatose patient who has altered level of alertness not attributable to sedation, in whom delirium cannot reliably be assessed because of the depressed alertness. Delirium, per DSM-5-TR, can only be diagnosed in patients who are sufficiently conscious to assess attention and awareness; thus, coma—defined as unarousable unresponsiveness—excludes a diagnosis of delirium until the patient regains consciousness. It is confusing to use different terms for the underlying substrate (encephalopathy) versus the clinical manifestations thereof (delirium). Oldham and Halloway discussed a theoretical model to highlight a clinical phenotype-related definition of delirium and an etiology-related definition of acute encephalopathies. To include both the clinical phenotype and the underlying brain disorder, the overarching term 'delirium disorder' has been introduced [3].

### Risk of long-term cognitive impairment

Delirium disorder is a well-established independent risk factor for long-term cognitive dysfunction, incident dementia and worsening of existing dementia [4]. In a study with high power, including 650,590 non-demented elderly, who were followed for more than 5 years, patients with delirium had 39% higher risk of death and a three times higher risk of incident dementia than those without delirium [5]. It should, however, be noted that an independent association does not necessarily represent causation.

An increasing number of studies underpins detrimental effects of acute encephalopathy that manifests as delirium. Several important and extensively studied domains

*Correspondence: katarzyna.kotfis@pum.edu.pl; a.slooter-3@umcutrecht.nl
[1] Department of Anesthesiology, Intensive Care and Pain Management, Pomeranian Medical University, Szczecin, Poland
[3] Department of Psychiatry, and Research School of Behavioural and Cognitive Neurosciences (BCN), University Medical Center Groningen, University of Groningen, Groningen, The Netherlands
Full author information is available at the end of the article

SHOUT
SHARE
IT

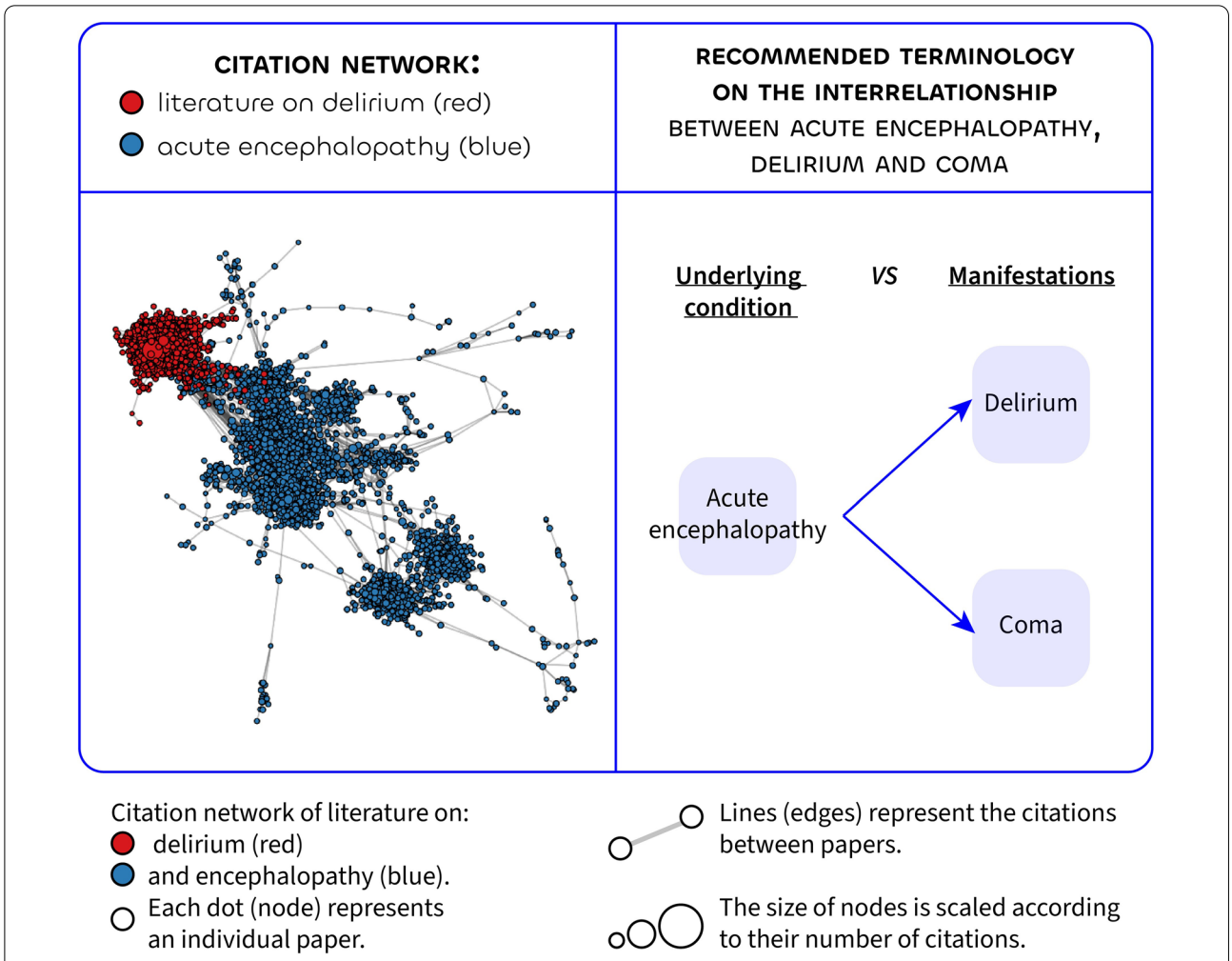
CITATION NETWORK:
literature on delirium (red)
acute encephalopathy (blue)
RECOMMENDED TERMINOLOGY ON THE INTERRELATIONSHIP BETWEEN ACUTE ENCEPHALOPATHY, DELIRIUM AND COMA
Underlying condition
VS
Manifestations
Delirium
Acute encephalopathy
Coma
Citation network of literature on:
delirium (red)
and encephalopathy (blue).
Each dot (node) represents an individual paper.
Lines (edges) represent the citations between papers.
The size of nodes is scaled according to their number of citations.

**Fig. 1** Citation network of literature on delirium (red) and encephalopathy (blue). Each dot (node) represents an individual paper. Lines (edges) represent the citations between papers. The size of nodes is scaled according to their number of citations. Node positioning is based on an iterative force directed layout algorithm which causes highly connected sets of nodes to cluster together. This figure shows that the literature on delirium and encephalopathy is highly segregated

have shown promising association with delirium—neuroinflammation, neuronal injury and neurotransmitter imbalance. To get an insight into more comprehensive understanding of the neurobiological mechanisms in this complex setting it is necessary to move beyond association and find true causal pathways [6]. Experimental research using animal models important, yet studies in humans are of critical importance [7, 8]. An approach using modern causal interference techniques, such as target trial emulation can be used to better analyze RCTs and establish this relationship.

#### Sedation-related and other phenotypes of delirium

Having said that acute encephalopathy is the pathobiological process in the brain, it is important to distinguish different phenotypes of ICU delirium as distinct clinical manifestations (i.e. hypoxic, septic, metabolic, sedative, unclassified) with a notion that sedation-related delirium differs from other types as it has different outcomes [9]. Factors such as sedative choice, depth of sedation, and the specific delirium assessment tool used are crucial in both clinical practice and research on sedation-related delirium, but other overlapping reasons should also be acknowledged (i.e., sepsis, electrolyte derangements, hypoxemia, central nervous system injury, alcohol intoxication or withdrawal, hyper or hypo-glycemia and extreme vitamin deficiencies).

Patel and colleagues evaluated patients in the context of delirium before and after sedatives were stopped. Despite methodological limitations (i.e., uncontrolled

design, limited adjustment for confounders, predominant use of propofol, and focus on short-term outcomes), the key contribution was the observation that rapidly reversible, sedation-related delirium may be associated with more favorable outcomes compared to other delirium subtypes as the patients with sedative-induced delirium had identical survival outcomes to those who had no ICU delirium at all [10].

Obviously, the treatment of these different reasons is founded in an understanding of the cause of delirium disorder.

## Future studies

Future studies should explore how emerging terminology—such as that proposed by Slooter et al.—can improve diagnostic accuracy, interdisciplinary communication, and the evaluation of patient outcomes such as long-term cognitive function, functional recovery, and quality of life [2].

Another pathway for future pragmatic studies lies within the need to train different medical specialties in understanding how new consensus-based, pragmatic nomenclature can challenge billing or reimbursement if different codes are used. Currently, it is financially more lucrative in the DRG system in the US to code an episode as 'encephalopathy' than as 'delirium', but efforts were made to achieve parity between delirium and acute encephalopathy in the MS-DRG system [11].

Moreover, more studies are needed to examine how clinical assessment of delirium aligns with EEG-based classification of acute encephalopathy, to determine whether EEG findings could offer added value to expert clinical evaluations. Research should focus on ways to distinguish between hypoactive delirium and non-delirious states or identify subclinical cases that may be missed during bedside assessment. Combining EEG markers of acute encephalopathy with clinical criteria for delirium may represent a promising reference framework for future research, particularly in the validation of delirium detection methods that incorporate EEG data and include AI-aided diagnostic tools [12–14].

Future research should also focus on long-term cognitive impairment and sedation-related delirium, as these are critical areas where knowledge gaps remain and where improved understanding could directly impact patient outcomes [6].

## Conclusion

Limitations of current terminology and the ongoing use of "encephalopathy" versus "delirium" in clinical practice and research dichotomizes the approach instead of unifying it. Expert panel regarded acute encephalopathy to be the pathobiological process in the brain, and delirium as a possible phenotypic manifestation of this process. Delirium disorder, including both clinical phenotype and underlying brain disorder, is a common problem in the ICU and perioperative care with substantial morbidity and mortality [4]. Although no randomized trials have directly tested the impact of ICU delirium screening or terminology improvement on outcomes, strong evidence from cohort studies—particularly those evaluating the ABCDEF bundle—supports routine delirium monitoring as part of comprehensive care. In line with the 2018 PADIS and 2024 ESAIC guidelines [15], regular screening should be considered standard practice to support early recognition and intervention.

**Author details**
[1] Department of Anesthesiology, Intensive Care and Pain Management, Pomeranian Medical University, Szczecin, Poland. [2] Pulmonary and Critical Care, University of Chicago Medical Center, Chicago, USA. [3] Department of Psychiatry, and Research School of Behavioural and Cognitive Neurosciences (BCN), University Medical Center Groningen, University of Groningen, Groningen, The Netherlands. [4] Department of Intensive Care Medicine and UMC Utrecht Brain Center, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands.

**Declarations**

**Conflicts of interest**
KK is a Section Editor for Intensive Care Medicine. She has not taken part in the review or selection process of this article.

**Ethics statement**
An approval by an ethics committee was not applicable.

**Open Access**
This article is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License, which permits any non-commercial use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by-nc/4.0/.

## Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Received: 29 April 2025 Accepted: 9 September 2025
Published online: 06 October 2025

**References**

1. Pandharipande PP, Girard TD, Jackson JC, Morandi A, Thompson JL, Pun BT, Brummel NE, Hughes CG, Vasilevskis EE, Shintani AK, Moons KG, Geevarghese SK, Canonico A, Hopkins RO, Bernard GR, Dittus RS, Ely EW, BRAIN-ICU Study Investigators (2013) Long-term cognitive impairment after critical illness. N Engl J Med 369(14):1306–1316. https://doi.org/10.1056/NEJMoa1301372

2. Slooter AJC, Otte WM, Devlin JW, Arora RC, Bleck TP, Claassen J, Duprey MS, Ely EW, Kaplan PW, Latronico N, Morandi A, Neufeld KJ, Sharshar T, MacLullich AMJ, Stevens RD (2020) Updated nomenclature of delirium and acute encephalopathy: statement of ten Societies. Intensive Care Med 46(5):1020–1022. https://doi.org/10.1007/s00134-019-05907-4. (**Epub 2020 Feb 13**)
3. Oldham MA, Holloway RG (2020) Delirium disorder: Integrating delirium and acute encephalopathy. Neurology 95(4):173–178. https://doi.org/10.1212/WNL.0000000000009949. (**Epub 2020 Jun 9**)
4. Wilson JE, Mart MF, Cunningham C, Shehabi Y, Girard TD, MacLullich AMJ, Slooter AJC, Ely EW (2020) Delirium. Nat Rev Dis Prim 6(1):90. https://doi.org/10.1038/s41572-020-00223-4
5. Gordon EH, Ward DD, Xiong H, Berkovsky S, Hubbard RE (2024) Delirium and incident dementia in hospital patients in New South Wales, Australia: retrospective cohort study. BMJ 384:e077634. https://doi.org/10.1136/bmj-2023-077634
6. Devlin JW, Sieber F, Akeju O, Khan BA, MacLullich AMJ, Marcantonio ER, Oh ES, Agar MR, Avelino-Silva TJ, Berger M, Burry L, Colantuoni EA, Evered LA, Girard TD, Han JH, Hosie A, Hughes C, Jones RN, Pandharipande PP, Subramanian B, Travison TG, van den Boogaard M, Inouye SK, Network for Investigation of Delirium: Unifying Scientists (NIDUS) Writing Group (2025) Advancing delirium treatment trials in older adults: recommendations for future trials from the network for investigation of delirium: unifying scientists (NIDUS). Crit Care Med 53(1):e15–e28. https://doi.org/10.1097/CCM.0000000000006514. (**Epub 2024 Nov 22**)
7. Kant IMJ, de Bresser J, van Montfort SJT, Witkamp TD, Walraad B, Spies CD, Hendrikse J, van Dellen E, Slooter AJC, BioCog Consortium (2023) Postoperative delirium is associated with grey matter brain volume loss. Brain Commun. 5(1):fcad013. https://doi.org/10.1093/braincomms/fcad013. (**eCollection 2023**)
8. Ditzel FL, van Montfort SJT, Vernooij LM, Kant IMJ, Aarts E, Spies CD, Hendrikse J, Slooter AJC, van Dellen E, Biomarker Development for Postoperative Cognitive Impairment in the Elderly Consortium (2023) Functional brain network and trail making test changes following major surgery and postoperative delirium: a prospective, multicentre, observational cohort study. Br J Anaesth 130(2):e281–e288. https://doi.org/10.1016/j.bja.2022.07.054. (**Epub 2022 Oct 17**)
9. Girad TD, Thompson JL, Pandharipande PP, Brummel NE, Jackson JC, Patel MB, Hughes CG, Chandrasekhar R, Pun BT, Boehm LM, Elstad MR, Goodman RB, Bernard GR, Dittus RS, Ely EW (2018) Clinical phenotypes of delirium during clinical illness severity of subsequent long-term cognitive impairment: a prospective cohort study. Lancet Respir Med 6(3):213–222. https://doi.org/10.1016/S2213-2600(18)30062-6
10. Patel SB, Poston JT, Pohlman A, Hall JB, Kress JP (2014) Rapidly reversible, sedation-related delirium versus persistent delirium in the intensive care unit. Am J Respir Crit Care Med 189(6):658–665. https://doi.org/10.1164/rccm.201310-1815OC
11. Oldham MA (2022) Follow the money: the widening coding disparity between acute encephalopathy and delirium. J Acad Consult Liaison Psychiatry. 63(5):423–425. https://doi.org/10.1016/j.jaclp.2022.02.004. (**Epub 2022 Feb 21**)
12. Numan T, Slooter AJC, van der Kooi AW, Hoekman AML, Suyker WJL, Stam CJ, van Dellen E (2017) Functional connectivity and network analysis during hypoactive delirium and recovery from anesthesia. Clin Neurophysiol 128(6):914–924. https://doi.org/10.1016/j.clinph.2017.02.022. (**Epub 2017 Mar 6**)
13. Hut SCA, Dijkstra-Kersten SMA, Numan T, Henriquez NRVR, Teunissen NW, van den Boogaard M, Leijten FS, Slooter AJC (2021) EEG and clinical assessment in delirium and acute encephalopathy. Psychiatry Clin Neurosci 75(8):265–266. https://doi.org/10.1111/pcn.13225. (**Epub 2021 Jun 9**)
14. Tesh RA, Sun H, Jing J, Westmeijer M, Neelagiri A, Rajan S, Krishnamurthy PV, Sikka P, Quadri SA, Leone MJ, Paixao L, Panneerselvam E, Eckhardt C, Struck AF, Kaplan PW, Akeju O, Jones D, Kimchi EY, Westover MB (2022) VE-CAM-S: visual EEG-based grading of delirium severity and associations with clinical outcomes. Crit Care Explor 4(1):e0611. https://doi.org/10.1097/CCE.0000000000000611
15. Aldecoa C, Bettelli G, Bilotta F, Sanders RD, Aceto P, Audisio R, Cherubini A, Cunningham C, Dabrowski W, Forookhi A, Gitti N, Immonen K, Kehlet H, Koch S, Kotfis K, Latronico N, MacLullich AMJ, Mevorach L, Mueller A, Neuner B, Piva S, Radtke F, Blaser AR, Renzi S, Romagnoli S, Schubert M, Slooter AJC, Tommasino C, Vasiljewa L, Weiss B, Yuerek F, Spies CD (2024) Update of the European Society of Anaesthesiology and Intensive Care Medicine evidence-based and consensus-based guideline on postoperative delirium in adult patients. Eur J Anaesthesiol 41(2):81–108. https://doi.org/10.1097/EJA.0000000000001876. (**Epub 2023 Aug 30**)